of individual test results around their average. Precision is usually expressed as percent relative standard deviation (% RSD) for a statistically significant number of samples. Both the FDA and the ICH recommend that precision be measured at three different levels. No such recommendation is given in the USP.

17.2.1. Repeatability

Repeatability expresses the results of the method operating over a short time interval under the same conditions. Repeatability is also termed intra-assay precision. According to the FDA Reviewer Guidance, repeatability is evaluated for injector performance and analysis of samples. For injector repeatability, there must be a minimum of 10 injections with an RSD of not more than ±1%. Similarly, with the methods for release and stability studies, an RSD of not more than ±1% for at least five injections for the active drug is desirable. For low-level impurities, higher variations in RSD may be acceptable. For analysis repeatability, determinations are made on multiple measurements of a sample by the same analyst under the same analytical conditions. The FDA recommends that the study be combined with accuracy.

The ICH recommends that repeatability should be determined from a minimum of nine determinations covering the specified range for the procedure (e.g., three levels, three replicates each), or from a minimum of six determinations at 100% of the test or target concentration. The target concentration is defined as the concentration of the compound of interest given in the analytical method.

17.2.2. Intermediate Precision

Intermediate precision expresses within-laboratory variations. This was previously evaluated as part of ruggedness. This attribute evaluates the reliability of the method in an environment different from that used during the method development phase. Depending on time and resources, the method can be evaluated on different days, with different analysts and equipment, etc. The FDA recommends performing accuracy on two separate occasions to indicate the intermediate precision of the test method. The ICH recommends using an experimental design (matrix) so that the effects, if any, of the individual variables on the analytical procedure can be monitored.

17.2.3. Reproducibility

Reproducibility is assessed by performing collaborative studies between laboratories. Multiple laboratories are desirable, if possible. According to the FDA Reviewer Guidance, reproducibility is not required if intermediate precision is achieved. The ICH recommends that reproducibility studies be performed for standardization of an analytical procedure, for instance, for inclusion of procedures to pharmacopoeias. The ICH also recommends that documents in support of each type of precision should include the standard deviation (S), the % RSD, the coefficient of variation, and the confidence interval.

17.3. Specificity/Selectivity

The terms specificity and selectivity are often used interchangeably. The term selectivity has been used in General Chapter <1225> of the 1990 edition of the